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SCIENTIFIC OPINION

Guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

The European Food Safety Authority (EFSA) asked the Panel on Dietetic Products, Nutrition and Allergies (NDA) to draft guidance on scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. This guidance has been drawn from scientific opinions of the NDA Panel on such health claims. Thus, this guidance document represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas. It is not intended that the document will include an exhaustive list of beneficial effects and studies/outcome measures which are acceptable. Rather, it presents examples drawn from evaluations already carried out in order to illustrate the approach of the Panel, as well as some examples which are currently under consideration within ongoing evaluations. A draft of this guidance document, endorsed by the NDA Panel on 25 March 2011, was released for public consultation from 26 April 2011 to 31 August 2011.

KEY WORDS

Health claims, scientific requirements, appetite, weight management, blood glucose.

[1] On request from EFSA, Question No EFSA-Q-2010-01183, adopted on 29 February 2012.

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BACKGROUND AS PROVIDED BY EFSA

Regulation (EC) No 1924/2006[4] harmonises the provisions that relate to nutrition and health claims and establishes rules governing the Community authorisation of health claims made on foods. According to the Regulation, health claims should only be authorised for use in the Community after a scientific assessment of the highest possible standard has been carried out by EFSA.

EFSA and its NDA Panel have been engaging in consultation with stakeholders and have published guidance on scientific substantiation of health claims since 2007[5]. Most recently, a briefing document on the scientific evaluation of health claims was published for consultation in April 2010, followed by a technical meeting with experts from the food industry, Member States and the European Commission in Parma, in June 2010[6].

Based on experiences gained with the evaluation of health claims, and to further assist applicants in preparing and submitting their applications for the authorisation of health claims, the NDA Panel is asked to develop guidance documents on the scientific requirements for the substantiation of health claims in selected areas, in addition to the guidance for the scientific substantiation of health claims related to gut and immune function (EFSA-Q-2010-01139).

TERMS OF REFERENCE AS PROVIDED BY EFSA

The NDA Panel is requested by EFSA to develop guidance documents on the scientific requirements for health claims in the following areas:

- Post-prandial blood glucose responses/blood glucose control
- Weight management, energy intake and satiety
- Protection against oxidative damage
- Cardiovascular health
- Bone, joints, and oral health
- Neurological and psychological functions
- Physical performance

Specific issues to be addressed in these guidance documents include:

- which claimed effects are considered to be beneficial physiological effects?
- which studies/outcome measures are appropriate for the substantiation of function claims and disease risk reduction claims?

Each guidance document should be subject to public consultation, and may be followed up as appropriate by scientific meetings with experts in the field.

Before the adoption of each guidance document by the NDA Panel the draft guidance shall be revised, taking into account the comments received during the public consultation. A report on the outcome of the public consultation for each guidance document shall be published. All guidance documents should be finalised by July 2012.

[4] Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.
[5] http://www.efsa.europa.eu/en/nda/ndaclaims.htm
[6] http://www.efsa.europa.eu/en/ndameetings/docs/nda100601-ax01.pdf

ASSESSMENT

1. Introduction

To assist applicants in preparing and submitting their applications for the authorisation of health claims, EFSA and in particular its Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA) has ongoing consultations with stakeholders, and has published guidance on the scientific substantiation of health claims since 2007[7]. In April 2010, a draft briefing document on the scientific evaluation of health claims was published for consultation and was followed by a technical meeting with experts from the food industry, Member States and the European Commission in Parma, in June 2010. The draft briefing document has been transformed into a Panel output, taking into account the questions/comments received. This document constitutes the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims, and outlines the approach of the NDA Panel to the evaluation of health claims in general. In response to requests from industry, EFSA is engaged in further consultation with stakeholders, and is developing additional guidance on specific types of claims.

The present guidance, prepared by the NDA Panel, on the scientific requirements for the substantiation of health claims related to appetite ratings, weight management, and blood glucose concentrations was, prior to its finalisation, endorsed by the NDA Panel on 25 March 2011 for public consultation, which was open from 26 April to 31 August 2011. All the public comments received that related to the remit of EFSA were assessed, and the guidance has been revised taking into consideration relevant comments. The comments received and a report on the outcome of the public consultation have been published on the EFSA website.

The document focuses on two key issues regarding the substantiation of health claims related to appetite ratings, weight management, and blood glucose concentrations:

- claimed effects which are considered to be beneficial physiological effects.
- studies/outcome measures which are considered to be appropriate for the substantiation of health claims.

Issues which are related to substantiation and which are common to health claims in general (e.g. characterisation of the food/constituent) are addressed in the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims [8].

This document has been drawn from scientific opinions of the NDA Panel on health claims related to appetite ratings, weight management, and blood glucose concentrations. Thus, it represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas. The document should be read in conjunction with the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims.

It is not intended that the document should include an exhaustive list of beneficial effects and studies/outcome measures which are acceptable. Rather, it presents examples drawn from evaluations already carried out in order to illustrate the approach of the Panel, as well as some examples which are currently under consideration within ongoing evaluations. Given that health claims are often technically complex and unique, additional health relationships and outcome measures for claimed

[7] http://www.efsa.europa.eu/en/ndaclaims/ndaguidelines.htm

[8] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. General guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. EFSA Journal, 9(4):2135, 24 pp.

effects need to be considered in the context of a specific application. This guidance document may be updated in the future in light of additional experience gained with the evaluation of health claims.

2. General considerations

2.1. Beneficial physiological effects

According to Regulation (EC) No 1924/2006, the use of health claims shall only be permitted if the food/constituent, for which the claim is made, has been shown to have a beneficial physiological effect. In assessing each claim, the NDA Panel makes a scientific judgement on whether the claimed effect is considered to be a beneficial physiological effect in the context of the specific claim, as described in the information provided and taking into account the population group for whom the claim is intended. For function claims, a beneficial effect may relate to maintenance or improvement of a function.

For reduction of disease risk claims, 'beneficial' refers to whether the claimed effect relates to the reduction (or beneficial alteration) of a risk factor for the development of a human disease (not reduction of the risk of disease). A risk factor is a factor associated with the risk of a disease that may serve as a predictor of development of that disease. Whether or not the alteration of a factor is considered to be beneficial in the context of a reduction of disease risk claim depends on the extent to which it is established that:

- The factor is an independent predictor of disease risk (such a predictor may be established from intervention and/or observational studies);
- The relationship of the factor to the development of the disease is biologically plausible.

Except for well established risk factors, the extent to which the reduction of a factor is beneficial in the context of a reduction of disease risk claim needs to be considered on a case-by-case basis.

The NDA Panel considers that the population group for which health claims are intended is the general (healthy) population or specific subgroups thereof, for example, elderly people, physically active subjects, or pregnant women. In its evaluation, the NDA Panel considers that where a health claim relates to a function/effect which may be associated with a disease, subjects with the disease are not the target population for the claim, for example, diabetic subjects. Applications for claims which specify target groups other than the general (healthy) population are the subject of ongoing discussions with the Commission and Member States with regard to their admissibility.

The NDA Panel also considers whether the claimed effect is sufficiently defined to establish that the studies identified for substantiation of the claim were performed with (an) appropriate outcome measure(s) of that claimed effect. Reference to general, non-specific benefits of the nutrient or food for overall good health or health-related well-being may only be made if accompanied by a specific health claim.

2.2. Studies/outcome measures appropriate for substantiation of claims

As human studies are central for the substantiation of health claims, this document focuses in particular on such studies. In considering whether the studies provided are pertinent (i.e. studies from which conclusions can be drawn for the scientific substantiation of the claim), the NDA Panel addresses a number of questions, including:

- Whether the studies have been carried out with the food/constituent for which the claim is made. This requirement means that there should be sufficient definition of the

food/constituent for which the claim is made, and of the food/constituent which has been investigated in the studies which have been provided for substantiation of the claim. The evaluation also considers how the conditions under which the human studies were performed relate to the conditions of use (e.g. quantity and pattern of consumption of the food/constituent) proposed for the claim.

- Whether the design and quality of the studies allow conclusions to be drawn for the scientific substantiation of the claim. The evaluation takes into account the hierarchy of evidence as described in the scientific and technical guidance of the EFSA NDA Panel[9], for example, intervention studies generally provide stronger evidence than observational studies. Intervention studies should be appropriately conducted so as to minimise bias. In observational studies, adequate control for factors other than the food/constituent which are known to have an impact on the claimed effect is important. Each health claim is assessed separately and there is no pre-established formula as to how many or what type of studies are needed to substantiate a claim. In this regard, the reproducibility of the effect of the food/constituent as indicated by consistency between studies is an important consideration.

- Whether the studies have been carried out in a study group representative of the population group for which the claim is intended. Can the results obtained in the studied population be extrapolated to the target population? For studies in groups (e.g. subjects with a disease) other than the target group for a claim (e.g. the general population), the NDA Panel considers on a case-by-case basis the extent to which it is established that extrapolation from the study group to the target group is biologically plausible.

- Whether the studies used (an) appropriate outcome measure(s) of the claimed effect. For this, the NDA Panel considers what is generally accepted in the relevant research fields (e.g. guidelines published by scientific societies based on rigorous methodological approaches), and consults experts from various disciplines, as appropriate.

3. Appetite ratings

Claims related to changes in appetite ratings (e.g. hunger, fullness, satiety, and desire to eat) after consumption of a food have been proposed. The beneficial physiological effect of changing appetite ratings depends on the context of the claim.

Claims on changes in appetite ratings have been made in the context of reducing body weight. In this context, evidence for a sustained effect on appetite ratings and on body weight with continuous consumption of the food should be provided (see Sections 4.1).

The scientific evidence for an effect on appetite ratings can be obtained from human intervention studies showing an increase in satiety/reduced sense of hunger or appetite (behavioural assessment) using methods with appropriate validity and precision (e.g. validated visual analogue scales). Evidence for a sustained effect with continuous consumption of the food should also be provided in order to exclude adaptation through compensatory mechanisms. Changes in certain biochemical markers (e.g. cholecystokinin (CCK)) may support the behavioural assessment.

Claims related to changes in appetite ratings after food consumption may be comparative claims (i.e. comparison of the "test" food with the "control" food). In this context, both the test and the control food should be sufficiently characterised for a scientific evaluation with respect to the factors (e.g. energy, volume, appearance and taste) which may have an impact on the claimed effect.

[9] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. Scientific and technical guidance for the preparation and presentation of an application for authorisation of a health claim (revision 1). EFSA Journal,9(5):2170, 36 pp.

Claims on other effects of changing appetite ratings in response to food consumption (e.g. effects on mood during energy restriction) should be specifically indicated and substantiated, and will be considered on a case-by-case basis.

4. Weight management

4.1. Claims related to the reduction of body fat/body weight

A sustained (intentional) reduction in total body fat is considered a beneficial physiological effect for adults in the general population with an excess of body fat. A reduction in body weight is also considered a beneficial physiological effect for adults with an excess body weight if body fat is reduced.

The scientific evidence for the substantiation of health claims on the reduction of body fat can be obtained from human intervention studies showing a reduction in total body fat using methods with appropriate validity and precision. Imaging techniques (e.g. dual energy X-ray absorptiometry (DEXA), magnetic resonance imaging (MRI) and computed tomography (CT)) are generally appropriate to assess changes in body fat in human intervention studies. Skinfold thickness, bioelectrical impedance analysis (BIA) and air displacement plethysmography (ADP) are generally not appropriate to assess small changes in body fat when used alone, particularly in obese subjects and/or when significant changes in body water compartments occur. Surrogate measures of total body fat (e.g. body weight) could be used for the scientific substantiation of these claims if the reduction in body weight is sufficiently large so that it could not be attributed to a reduction in lean body mass/body water.

The scientific evidence for the substantiation of health claims on the reduction of body weight can be obtained from human intervention studies showing a reduction in body weight which could not be attributed to a reduction in lean body mass/body water.

The conditions in which the effect on body fat/body weight is achieved need to be specified (under energy-restriction, eating *ad libitum*, etc.). Evidence for a sustained effect with continuous consumption of the food/constituent over, for example, about 12 weeks, should also be provided.

With respect to the study population, results from studies conducted in overweight or obese subjects treated with lifestyle measures only (e.g. diet and physical activity) could be used for the scientific substantiation of these claims. However, the rationale for extrapolation of results obtained in obese subjects under treatment with medications for weight loss (e.g. inhibitors of intestinal fat absorption and modifiers of central nervous system neurotransmitters) to the target population for the claim should be provided, and will be considered on a case-by-case basis (e.g. evidence for a lack of interaction between the food and the medications used on the claimed effect).

Changes in appetite ratings, energy intake, energy expenditure or fat oxidation have been proposed in the context of claims related to the reduction of body fat/body weight. Evidence for a sustained effect on any of these variables with continuous consumption of the food (in order to exclude adaptation) may be considered in support of the mechanisms by which the food may exert the claimed effect.

4.2. Claims on body weight maintenance after weight loss

The scientific evidence for the substantiation of health claims related to the maintenance of body weight after (intentional) weight loss can be obtained from human intervention studies showing an effect on (limiting) body weight regain after significant weight loss. The conditions in which the effect is achieved need to be specified (under energy-restriction, eating *ad libitum*, etc.). Evidence for

a sustained effect with continuous consumption of the food/constituent over, for example, about six months, should also be provided.

4.3. Claims related to the reduction of abdominal fat

A sustained reduction in abdominal fat, and particularly in visceral fat, is considered a beneficial physiological effect for adults with adverse health effects associated with an excess of abdominal fat (e.g. impaired glucose tolerance, dyslipidaemia and high blood pressure).

The scientific evidence for the substantiation of health claims related to the reduction of abdominal fat can be obtained from human intervention studies showing a reduction in abdominal fat by using methods with appropriate validity and precision (e.g. MRI and CT). Surrogate measures of abdominal fat (e.g. waist circumference) could be used for the scientific substantiation of these claims if the reduction is sufficiently large so that it could not be attributed to a reduction in lean body mass/body water. The conditions in which the effect is achieved need to be specified (under energy-restriction, eating *ad libitum*, etc.). Evidence for a sustained effect with continuous consumption of the food/constituent over, for example, about 12 weeks, should also be provided.

4.4. Claims on the increase/maintenance of lean body mass

A sustained increase in lean body mass may be a beneficial physiological effect for physically active subjects, including trained individuals. The maintenance (i.e. reduced loss) of lean body mass may also be beneficial, for example, during energy restriction leading to weight loss, or for older adults.

The scientific evidence for the substantiation of health claims on the increase/maintenance of lean body mass can be obtained from human intervention studies showing an increase (or reduced loss) in lean body mass which could not be attributed to an increase in body weight (i.e. an increase in lean body mass relative to body fat mass). Changes in lean body mass should be assessed using methods with appropriate validity and precision. Imaging techniques (e.g. DEXA, MRI and CT) are generally appropriate to assess changes in lean body mass in human intervention studies. BIA and ADP may not be appropriate to assess small changes in lean body mass when used alone, particularly in obese subjects and/or when significant changes in body water compartments occur. The conditions in which the effect is achieved need to be specified (e.g. training vs. usual physical activity, eating *ad libitum* vs. energy-restriction, etc.). Evidence for a sustained effect with continuous consumption of the food/constituent over, for example, about 12 weeks, should also be provided. Measurements of protein metabolism (e.g. synthesis and breakdown) may be used in support of a mechanism by which the food/constituent could exert the claimed effect.

5. Blood glucose and insulin concentrations

5.1. Claims on the reduction of post-prandial blood glucose responses

Claims on the reduction of post-prandial blood glucose responses refer to the ability of a food/constituent to reduce the blood glucose rise after consumption of a food or meal rich in digestible carbohydrates (i.e. in comparison to a reference food or meal). This ability may be considered a beneficial physiological effect (e.g. for subjects with impaired glucose tolerance) as long as insulin responses are not disproportionally increased.

The scientific evidence for the substantiation of health claims on the reduction of post-prandial blood glucose responses can be obtained from human intervention studies showing a decrease in blood glucose concentrations at different time points after consumption of the test food during an

appropriate period of time (i.e. at least two hours) and no increase in insulin concentrations in comparison to the reference food.

Claims have been proposed for food constituents which, when present in carbohydrate-containing foods (e.g. different types of dietary fibre), could reduce post-prandial blood glucose responses to such foods by, for example, decreasing the rate of absorption of available carbohydrates. In this context, both the test and the reference food should be sufficiently characterised for a scientific evaluation and comparable with respect to factors other than the food constituent responsible for the claimed effect (e.g. amount of available carbohydrates, fat and protein content).

Claims for a beneficial effect of a food/constituent (e.g. non/low-digestible carbohydrates, intense sweeteners and sugar alcohols), when used in replacement of another food/constituent (e.g. digestible carbohydrates) with an independent role in increasing post-prandial glycaemic responses, have been proposed. Substantiation may be based on evidence for an independent role of the replaced food/constituent in increasing post-prandial glycaemic responses, together with evidence for the lack of such an effect, or a reduced effect, of the food/constituent which is used for replacement.

With respect to the study population, results from studies conducted in diabetic subjects treated with lifestyle measures only (e.g. diet and physical activity) could be used for the scientific substantiation of these claims. However, the rationale for the extrapolation of results obtained in diabetic subjects under treatment with blood glucose-lowering medications (e.g. oral anti-diabetic medications and insulin) to the target population for the claim (e.g. the general population or subjects with impaired glucose control) should be provided, and will be considered on a case-by-case basis (e.g. evidence for a lack of interaction between the food/constituent and the medications used on the claimed effect).

5.2. Claims on (long-term) maintenance of normal blood glucose concentrations

Maintenance of normal blood glucose concentrations is considered a beneficial physiological effect.

The scientific evidence for the substantiation of health claims on the long-term maintenance of normal blood glucose concentrations can be obtained from human intervention studies showing an improved blood glucose control assessed by changes in glycated haemoglobin (HbA1c). Evidence for a sustained effect with continuous consumption of the food/constituent over at least 12 weeks should be provided. Measurements of plasma glucose concentrations after a standard oral glucose tolerance test (OGTT) and measurements of fructosamine can be considered as supportive evidence. Changes in insulin sensitivity assessed using appropriate (dynamic) outcome measures (e.g. hyperinsulinaemic-euglycaemic clamp, the insulin sensitivity index (ISI) and the quantitative insulin sensitivity check index (QUICKI)) could be used in support of a mechanism by which the food/constituent could exert the claimed effect.

With respect to the study population, results from studies conducted in diabetic subjects treated with lifestyle measures only (e.g. diet and physical activity) could be used for the scientific substantiation of these claims. However, the rationale for extrapolation of results obtained in diabetic subjects under treatment with blood glucose-lowering medications (e.g. oral anti-diabetic drugs and insulin) to the target population for the claim (e.g. the general population or subjects with impaired glucose control) should be provided, and will be considered on a case-by-case basis (e.g. evidence for a lack of interaction between the food/constituent and the medications used on the claimed effect).

CONCLUSIONS

The draft guidance document has focused on two key issues regarding the substantiation of health claims related to appetite ratings, weight management, and blood glucose concentrations:

- claimed effects which are considered to be beneficial physiological effects.
- studies/outcome measures which are considered to be appropriate for the substantiation of health claims.

The document has been drawn from scientific opinions of the NDA Panel on health claims related to appetite ratings, weight management, and blood glucose concentrations. Thus, it represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas.

GLOSSARY AND ABBREVIATIONS

ADP	Air displacement plethysmography
BIA	Bioelectrical impedance analysis
CCK	Cholecystokinin
CT	Computed tomography
DEXA	Dual energy X-ray absorptiometry
HbA1c	Glycated haemoglobin
ISI	Insulin sensitivity index
MRI	Magnetic resonance imaging
OGTT	Oral glucose tolerance test
QUICKI	Quantitative insulin sensitivity check index